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The role of nutritional support in cirrhotic patients

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Abstact

Malnutrition is usual in patients with chronic liver disease and is associated with a poor outcome. Nutritional support decreases nutrition-associated complications. Our aim was to demonstrate that nutritional support in cirrhotic patients leads to early and better recovery. Two hundred and fifty patients with cirrhosis were included and followed for six months. Two hundred subjects (Group A) received fat rich diet having nutritional value of 35 Kcal/kg/day and 1.5 gm/kg/day of vegetable protein. Fifty patients (Group B) did not give consent for above diet and remained on low calorie, fat and protein restricted diet. Fifteen patients (7.5%) in Group A died whereas eight (16%) patients in Group B died. The mean average hospital stay in group A was 11 days whereas in Group B it was 18 days. All the complications were less common in Group A then in Group B patients. Good nutritional support in cirrhotic patients decreases mortality and morbidity.

Key words: Malnutrition, Cirrhosis, Anthropometry, liver function tests

Introduction

Malnutrition is invariably present in advanced stages of liver damage (Mendenhall etal 1984; Bollet 1973; Bunout, 1989; Hirsch etal 1993). Several factors such as anorexia, alterations in protein and energy metabolism, increased fat oxidation, alcohol ingestion, dietary restrictions or nutrient malabsortion have been implicated in the deterioration of nutritional status (Cabre 1993). Nitrogen balances are often negative in chronic liver disease (CLD) due to low protein ingestion or absorption and increased protein catabolism (McCullough 1992; McCullough etal 1992). Protein turnover studies have found increased protein catabolism associated with coexisting events, such as alcohol ingestion, infections and stress (Hirsch 1995 Marchesini etal 1992), rather than in stable conditions (Muller, 1986; Dichi etal, 1996). Concerning energy metabolism, low (Merli etal 1990), normal (Owen 1983; Jhangiani etal 1986) or high energy expenditure has been reported in cirrhotic patients (Shanbhogue 1987; Riggio etal 1992). In a large study, hyper metabolism was found to be associated with concurrent conditions, so it cannot be considered a constant feature of cirrhosis (Muller 1992). Interestingly, high volume ascites seems to increase resting metabolic rate, since it decreases after Ascites removal (Dolz etal 1991).Nutrition critically affects the immune system, involving both the antigen-nonspecific and the adaptive or antigen-specific responses. Several investigations have confirmed the adverse effects of protein-energy malnutrition (PEM) over different aspects of host defenses (Santos 1994) and probably also the gut barrier (Deitch 1994; Edmiston1991; Welsch etal 1998). Interestingly, it has been demonstrated that immune alterations recover with nutritional replenishment (Gefhyusen 1971)].As malnutrition adversely affects the outcome of many chronic and acute diseases (Reinharst 1981,Barga etal 1988;Mendenhall 1986), numerous trials have attempted to correct nutritional status in CLD, hoping to decrease morbidity and mortality (Nasrallah 1980; Nompleggi 1994).Thus, our aim was to demonstrate that good nutritional diet decreases morbidity and mortality in cirrhotic patients.

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Patients and methods

Patients attending liver disease clinic were considered eligible for this study if they had clinical, biochemical and radiological evidence of cirrhosis. The study was approved by local ethical committee of Post Graduate Institute of Medical Sciences which is affiliated to University of Health Sciences, Rohtak, Haryana, and all eligible patients signed a written informed consent. Two hundred and fifty patients with cirrhosis were included. Two hundred subjects (Group A) received fat rich diet having nutritional value of 35 Kcal/kg/day ,1.5 gm/kg/day of vegetable protein, 2-4 gm/day salt and total 1.5 liters of fluid intake per day. Liver function tests were done at regular intervals. Fifty patients (Group B) did not give consent for above diet and remained on low calorie, fat and protein restricted diet. The drug treatment was same in both the groups. Patients were initially admitted in indoor ward of Gastroenterology department and later on followed on OPD

basis twice monthly. On each visit, they were clinically examined and detailed biochemical profile including complete haemogram, erythrocyte sedimentation rate ,total proteins, albumin, creatinine, blood urea nitrogen, blood sugar total bilirubin, alkaline phosphatase, aspartate & alanine aminotransferase and prothrombin time were done in addition to ultrasound abdomen. They were asked about pharmacological treatment received, alcohol ingestion and compliance with the nutritional diet intake (nutritionist assessed the total dietary intake). In our study, none of patient was given enteral products. Subjects were examined at entrance to the study and monthly or more frequently, if necessary, during a six month period. Every third month, a complete clinical and nutritional assessment was performed, including anthropometric measurements (weight, midarm circumference, triceps skin fold thickness using a Lange caliper at four standard locations).

RESULTS

Two hundred and fifty patients of proven chronic liver disease were enrolled in the present study. Two hundred patients who gave consent for nutritionally rich diet were included in group A whereas fifty patients who denied were allotted group B. The baseline nutritional parameters, as shown in Table 1, in both the groups were comparable and did not have any statistically significant variation.

Table 1. Initial nutritional features of all patients (n = 250)

	Group A	200 Patients	Group B	50 Patients
	Mean & STD	Range	Mean & STD	Range
Age (Years)	46.23 , 7.1	30-64	45.8, 6.9	29-63
Weight(kg)	63.12 , 11.4	47.5-98	65.5 , 10.8	51-100
Height(cm)	164.22 , 5.7	154-175	164.5 , 5.1	150-173
Triceps skin fold (mm)	10.6 , 5.7	6-27	10.1 , 5.8	6- 29
Mid-arm circumference (cm)	25.8 , 3.9	20.5-29.5	25.9 , 4.1	21-30

Table 2. Initial biochemical parameters of all patients (n=250)

	Group A	200 Patients	Group B	50 Patients
	Mean	Range	Mean	Range
Serum proteins (g/dL)	6.8	5-7.6	6.6	4.9-7.3
Serum albumin (g/dL)	3.0	2.2-4.3	3.1	1.9-4.1
Serum creatinine (mg)	1.3	0.7-2.7	1.5	0.8-1.9
Total bilirubin (mg %)	3.1	0.6-10.2	2.9	1-9.4
AST (I.U)	87	47-218	90	54-210
ALT (I.U)	65	23-198	63	25-92
ALP (I.U)	187	67-235	190	54-212
Hemoglobin (gm %)	9.8	7.1-11.3	10.1	7.5-10.8
ESR(mm/h)	43.5	32-75	45.5	29-78
TLC	7100	4100-17300	7700	4200-16900
Platelet count (lakh/mm3)	0.9	0.7-2.3	0.98	0.81-2.6

After 3 months follow up.

The follow up of patients clearly proved that patient in Group A who were getting good diet as planned had gain in weight, mid-arm circumference and triceps fold thickness in comparison to patients in Group B who in contrast had decline in all the above parameters.

Table 3. Nutritional Features of All Patients (n = 250) after 3 months

	Group A	200 Patients	Group B	50 Patients
	Mean & STD	Range	Mean & STD	Range
Age (Years)	46.23 , 7.1	30-64	45.8, 6.9	29-63
Weight (kg)	65.20 , 10.8	50-101	66 , 10.4	52-100
Height (cm)	164.22 , 5.7	154-175	164.5 , 5.1	150-173
Triceps skin fold (mm)	11.7 , 5.3	6.7-29	9.8 , 5.9	5.8- 28
Mid-arm circumference (cm)	27 , 3.7	21.5-31.3	24.8 , 4.3	20-28.8

During these three months of follow up, there was increase in Serum protein, Serum albumin and hemoglobin levels but it was distinctly more in Group A than in Group B. There was decrease in Serum bilirubin, AST, ALT, ALP and ESR levels in both the groups but it was more significantly decreased in Group A in comparison to Group B. The serum creatinine, total leukocyte and platelet count had not much alteration in both the groups during these three months of follow up.

Table 4. Biochemical parameters of All patients (n=250) after 3 months

	Group A	200 Patients	Group B	50 Patients
	Mean	Range	Mean	Range
Serum proteins (g/dL)	7.5	5.2-8.6	6.8	5.1-7.4
Serum albumin (g/dL)	3.4	2.6-4.7	3.2	2.1-4.3
Serum creatinine (mg)	1.2	0.7-2.5	1.4	0.9-1.9
Total bilirubin (mg %)	2.3	0.6-4.9	2.6	0.8-5.1
AST(I.U)	75	40-118	85	47-190
ALT(I.U)	58	22-112	60	23-88
ALP(I.U)	170	60-215	181	50-203
Hemoglobin (gm %)	10.2	7.5-11.8	10.2	7.7-10.9
ESR (mm/h)	40.5	28-65	42.5	27-70
TLC	7000	4300-14000	7500	4300-14200
Platelet count (lakh/mm3)	0.98	0.8-2.5	0.99	0.84-2.8

After 6 months follow up.

The follow up after six months further showed that patient in Group A who were getting good diet as planned had gain in weight, mid-arm circumference and triceps fold thickness in comparison to patients in Group B who in contrast had almost decline in all the above parameters.

Table 5. Nutritional Features of All Patients (n = 250) after 6 months

	Group A	**200 Patients**	**Group B**	**50 Patients**
	Mean & STD	**Range**	**Mean & STD**	**Range**
Age (Years)	46.23 , 7.1	30-64	45.8, 6.9	29-63
Weight(kg)	66.75 , 11.2	51-102	66.3 , 10.6	50.5-99.5
Height(cm)	164.22 , 5.7	154-175	164.5 , 5.1	150-173
Triceps skin fold (mm)	12.3 , 5.6	7-28.5	9.6 , 5.5	5.5- 27.5
Mid-arm circumference (cm)	28.3 , 3.5	22.2-31.9	24.2 , 4.0	20-28

During these six months of follow up, there was increase in Serum protein, Serum albumin and hemoglobin levels but it was distinctly more in Group A than in Group B. There was decrease in Serum bilirubin, AST, ALT, ALP and ESR levels in both the groups but it was more significantly decreased in Group A in comparison to Group B. The serum creatinine, total leukocyte and platelet count had not much alteration in both the groups during these six months of follow up.

Table 6. Biochemical parameters of all patients (n=250) after 6 months

	Group A	**Group B**
Total Infective Episodes	65 (26%)	20 (40%)
Spontaneous Bacterial Peritonitis	25 (38.46% of total infective episodes)	11 (55% of total infective episodes)
Episodes of G.I. bleed	18 (7.2%)	6 (12%)
Episodes of Porto systemic Encephalopathy	17 (6.8 %)	5 (10%)
Episodes of Hepatorenal syndrome	13 (5.2%)	4 (8%)
Total Number of Deaths	15 (7.5%)	8 (16%)
Mean Average Hospital stay	11 days (range 7-16 days)	18 days (11-24 days)

	Group A	**200 Patients**	**Group B**	**50 Patients**
	Mean	**Range**	**Mean**	**Range**
Serum proteins (g/dL)	7.8	5.4-8.8	6.9	5.2-7.6
Serum albumin (g/dL)	3.6	2.8-4.9	3.3	2.2-4.4
Serum creatinine (mg)	1.25	0.8-2.0	1.3	0.9-1.7
Total bilirubin (mg %)	2.1	0.6-4.1	2.3	0.7-3.0
AST (I.U)	70	40-108	78	43-120
ALT (I.U)	52	24-82	53	23-80
ALP (I.U)	166	53-185	175	48-193
Hemoglobin (gm%)	10.6	7.8-12.0	10.3	7.8-11.1
ESR (mm/h)	33.5	20-45	39.5	24-52
TLC	7150	4500-11000	7400	4400-13000
Platelet count (lakh/mm3)	1.1	0.85-2.8	1.01	0.85-3.0

When we compared morbidity and mortality rates in the above two groups, patients in Group A outscored the patients in Group B in all aspects. The morbidity and mortality was less in Group A as compared to Group B.

Discussion

Malnutrition is commonly seen in both alcoholic and nonalcoholic liver disease (Italian multicentre trial 1994; Caregaro 1996; Campillo 2003) and has been shown to adversely affect outcome (Kolman 1992; Alberino 2001). By definition, it occurs when diet does not provide adequate calories and protein to maintain nutritional status or the body is unable to fully absorb or utilize food eaten secondary to liver disease. Despite the obvious relevance, clinical research in this field is limited and malnutrition is frequently under diagnosed in clinical practice (Cabre 1998). The prevalence of malnutrition in cirrhosis is as high as 65%–90% . Evidence concerning the impact of etiology (of cirrhosis) on malnutrition is conflicting. Some studies have shown no difference in prevalence and severity of malnutrition in patients with viral- and alcohol related cirrhosis that was abstinent. Others have shown that alcoholic cirrhosis was associated with a poorer nutritional state compared with virus-associated cirrhosis. Active alcoholism is a major cause of malnutrition per se and could contribute to the earlier development observed (Thuluvath 1994). Protein depletion and reduced muscle function are common in cirrhosis, particularly in men and patients with alcoholic liver disease (Sarin etal 1997). The reason for the male preponderance is unknown and is not related to hypermetabolism or reduced energy and protein intake (Caly 2003).The reduced levels of testosterone observed in male patients with cirrhosis (Simko 1982) may contribute to decreased protein anabolism, but this requires further investigation. The largest studies on prevalence and severity have been the Veterans Affairs Cooperative Studies in 1984 and 1993, which focused on alcoholic hepatitis (Peng 2007; Baker etal 1976). These and other studies showed that the severity of malnutrition correlated with that of the liver disease and the development of serious complications such as hepatic encephalopathy, ascites, hepatorenal syndrome, post transplantation outcome, and mortality (Mendenhall etal 1984,1983; Pikul 1994; Harrison 1997). Also, short term survival is reduced in parallel with severity of malnutrition (Moller etal 1984; Mendenhall 1995; Mendenhall etal 1986). In our study also we compare all these parameters in two groups and results are in line with these studies i.e. in Group A patients who received good nutritious diet, all complications like Infections, Spontaneous bacterial peritonitis, Porto-systemic encephalopathy, Hepatorenal syndrome, hospital stay and deaths were less in comparison to Group B who willingly received nutrition restricted diet.

Malnutrition, regardless of its causes, can lead to liver damage and impaired liver function. For example, children in underdeveloped countries whose diets do not contain enough protein can develop a disease called kwashiorkor. One symptom of this disorder is the accumulation of fat in the liver, a condition known as fatty liver. Studies performed during and after World War II indicated that severe malnutrition also could lead to liver injury in adults. However, in these cases other factors, including exposure to certain toxins or parasites that are prevalent in war-ravaged or underdeveloped countries, may have exacerbated the relationship between liver injury and poor nutrition. Good nutritious diet improves cellular

immunity and nutritional status in cirrhotic patients. This has been clearly demonstrated in various studies. Cirrhosis and alcoholism are both associated with immunological changes. Alcohol consumption appears to attenuate the production and migration of polymorphonuclear leukocytes and inhibits cell-mediated immunity. Cirrhosis is associated with a lower T lymphocyte count, cutaneous anergy, and chemotactic activity disturbances, decreased complement factors and depressed macrophage phagocytic activity. These changes are very similar to those caused by protein energy malnutrition (Chandra etal 1983, 1987) Bacterial translocation and intestinal permeability is increased in animal models of cirrhosis (Bersky 1987; Adachi 1995, Llovet etal 1994). Other causes of elevated intestinal permeability are malnutrition and the metabolic response to injury (Bjaneson 1993). Bacterial translocation is associated with a higher risk of developing gut derived infections such as spontaneous bacterial peritonitis and bacteraemia. It also activates phagocytic cells to produce lymphokines, whose adverse effects can perpetuate liver damage or induce wasting. Although endotoxemia is common in cirrhotic patients with portal hypertension (Lumsden 1981; Bode 1997), intestinal permeability has been reported to be normal (Budillon 1985). An enhanced production of these cytokines is associated with acute events such as infections and acute alcoholic hepatitis. IL-6 is elevated in patients with chronic liver disease, associated with ascites and end stage cirrhosis (Khoruts 1991; Nepali 1994; Byl 1994; Prospt 1993). Serum albumin levels increased during the nutritional intervention. However, this parameter is not a sensitive indicator of visceral protein storage in cirrhotic patients. Albumin concentrations levels are a function of its rate of synthesis, volume of distribution and catabolism. The causes of hypoalbuminemia in cirrhotic subjects are an enlarged volume of distribution and increased catabolic rate, without a compensatory increase in albumin synthesis, due to inadequate synthetic reserve, inadequate protein intake and frequent superimposed infections. Volume depletion due to a more efficient ascites management could also play a role.

Conclusion

Malnutrition is common in end stage liver disease and adversely affects prognosis. The nutritional support in cirrhotic patients improves nutritional status and host defenses due to better cellular immunity and less intestinal bacterial overgrowth Nutritional support improves outcome in patients unable to maintain an intake of 35–40 kcal / kg/ day and 1.2–1.5 g/ kg/ day of protein. Simple methods of assessment such as subjective global assessment, midarm muscle circumference, and calorie counting are useful, and standard enteral products may be used to achieve the target ,if we are not able to achieve required total calories and protein intake by oral route.

Recommendations

The most common and difficult to handle myth about liver disease is that there should be almost complete restriction of dietary fat and protein intake in diet, which is in contrast to the actual scientific dietary advices for such patients. Hence we should regularly and persistently convince the patient and relatives to give high protein and fat diet with less of salt , as decided upon degree of decompensation.

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